REMARKS UNDER 37 CFR § 1.111

Formal Matters

Claims 1, 3 and 5-18 are now pending in this application.

Claims 2 and 4 have been canceled.

Claims 1, 6, 8, 10, 12 and 18 have been amended to more particularly point out and distinctly claim the invention.

Claim 1 has been amended to clearly recite the step of "evaluating renal function" in the body of the claim thereby conforming the body of the claim to the claim preamble. Claim 1 has also been amended to incorporate language contained within claim 2. Specifically, claim 1 now includes the steps required to correlate the megsin protein amount and renal function. Original claim 2 has been canceled. Claim 1 has also been amended to refer to "a control specimen from a healthy individual" as supported in the specification such as at page 16, lines 22-27.

Claims 6, 8 and 12 have been amended to refer to the specific sequence numbers SEQ ID NOS.:11, 12, 14 and 17. This amendment is supported within the original specification such as in examples 2, 7 and 10-13.

Claim 10 has been amended to replace the term "relative density" with the term --specific gravity-- as supported in the specification such as at page 23, lines 15-21.

Claim 12 has been amended to more clearly recite the relationship between the first and second anti-megsin protein antibody and the analyte (megsin protein). This amendment is supported within the original specification such as at page 12, lines 27-32.

No new matter has been added.

Objections to the Specification

The Examiner objected to the specification at page 1, line 23. Although applicant is amenable to amending the specification the current terminology is well accepted internationally. The term is intended to mean a cost of 6,000,000 yen and the specification is currently correctly written to recite such using "¥" for "yen". If for some reason the Examiner would prefer different technology after this explanation applicant is amendable to amending the specification. However, in view of this explanation this objection is believed to have been overcome.

Rejection over 35 U.S.C. §112, second paragraph

Claims 1-3, 5, 10 and 13-16 were rejected under 35 U.S.C. §112 as being indefinite. The rejection is traversed as applied and as it might be applied to the presently pending claims.

Applicant has amended claim 1 to clearly recite "evaluating renal function" language in the body of the claim. Further, claim 1 has been amended to clearly correlate the megsin protein amount to renal function by reciting the steps a, b, c and d. In view of these amendments the rejection as applied to claim 1 is believed to have been overcome.

The rejection also argued that the term "normal specimen" is indefinite. In view of such applicant has canceled claim 2 and included other language supported within the specification into amended claim 1. Specifically, applicant refers to "a control specimen from a healthy individual" instead of a "normal specimen" in amended claim 1. Within the specification at page 16, lines 22-27 applicant describes that the renal function can be evaluated using a megsin protein amount of a normal healthy person as a control.

The rejection also indicated that claim 10 was unclear but the basis of the rejection was not pointed out. However, applicant has attempted to further clarify the claim by deleting the term "relative density" and adding –specific gravity—as supported in the specification at page 23, lines 15-21. It is applicant's position that the two expressions have the same meaning. If this amendment remains objectionable to the Examiner for whatever reason applicant would be amenable to other amendments in order to clarify the claimed invention.

Claim 12 was rejected arguing that the relationship between the granule and marker molecule was not clear. Applicant has amended claim 12 to clarify that both the first antibody on the granule and the second antibody labeled with the marker molecule bind to the analyte which is megsin protein.

In view of the above the 35 U.S.C. §112, second paragraph rejections are believed to have been overcome and an indication of such is respectfully requested.

Rejection under 35 U.S.C. §102

Claims 6 and 7 were rejected under 35 U.S.C. §102 as anticipated by Tsujimoto. In support of the rejection it was argued that Tsujimoto et al. disclosed a protein comprised of 380 amino acids and monoclonal antibodies directed thereto. It was argued that even though Tsujimoto et al. do not explicitly state that the protein is megsin, it is inherent that the amino acid residue constitutes the megsin protein,

and therefore, monoclonal antibodies disclosed by Tsujimoto et al. anticipate the invention claims within previously pending claims 6 and 7.

The antibodies disclosed by Tsujimoto et al. are different from those recited within the present application. Claim 6 has been amended to refer to specific amino acid sequences of antigens which are not disclosed within Tsujimoto. Accordingly, the 35 U.S.C. §102 rejection is overcome.

To the extent that a 35 U.S.C. §103 might be applied applicant points out that in the first paragraph on page 15377 of Tsujimoto et al. that the monoclonal antibodies are prepared by raising them against the whole amino acid sequence of the megsin protein. However, the megsin protein antibodies of the present invention are prepared using partial peptides of megsin protein as the immunogens. In support of such applicant specifically refers to Example 2. In order to emphasize the difference in immunogens claim 6 has been amended as have claims 8 and 12 in order to refer to the anti-megsin protein antibodies of the present invention raised against the amino acid sequences of SEQ ID NOS: 11, 12, 14 or 17. In that Tsujimoto et al. did not disclose or suggest antibodies against partial peptides of megsin protein the presently claimed antibodies are not believed to be obvious in view of Tsujimoto. Accordingly, claims 6 and 7 are believed to be patentable over the cited art.

Rejection under 35 U.S.C. §103

Claims 1, 2, 5-9, and 11-8 were rejected under 35 U.S.C. §103 as unpatentable over Gombinski in view of Tsujimoto et al. The rejection is traversed as applied and as it might be applied to the presently pending claims. Amended claims 1, 2 and 5 are directed to a method for (1) detecting or measuring megsin protein; and (2) evaluating renal function using a measured value for megsin protein. Accordingly, one skilled in the art would not be led to the present invention by merely combining the Gombinski and Tsujimoto et al. references. Claim 1 requires that megsin protein be measured and renal function be evaluated by comparing the amount of megsin protein measured with that of a healthy individual. Applicant was the first to recognize that it is possible to evaluate renal function by first detecting and measuring megsin protein and then using that measurement to evaluate renal function by comparing it with a controlled specimen from a controlled individual. Neither Tsujimoto et al. or Gombinski teach or suggest this comparison step. In the absence of any teaching toward such it is applicant's position that amended claim 1 as well as claims 2, 5-9 and 11-18 are patentable over any combination of Gombinski and Tsujimoto et al. Further, it is applicant's position that it would not

obvious for one of ordinary skill in the art to combine Gombinski and Tsujimoto et al. in the absence of applicant's teachings.

Above applicant has pointed out that the antibodies raised against the fragments of megsin protein are different from those taught within Tsujimoto et al. Accordingly, with respect to any of claims 6-7, 8-11, 12-16, and 17-18 applicant has utilized antibodies which are not taught within Tsujimoto et al. Accordingly, even if Tsujimoto et al. is combined with Gombinski it does not teach the claimed invention. This is because the antibodies of Tsujimoto et al. are raised against the entire protein as the immunogen. Applicant has utilized partial peptides of the megsin protein which show low identity with other members of the serpin family and are hydrophilic as immunogens. This is pointed out within Example 2. Tsujimoto et al. do not disclose or suggest the use of fragments of the megsin protein as an immunogen. Specifically, Tsujimoto et al. do not suggest specific fragments of the protein to be used as the immunogen in order to obtain antibodies to detect megsin protein in a biological sample. Accordingly, even when the teachings of the Tsujimoto et al. are combined with the Gombinski the claimed invention is not obtained.

Rejection over Tsujimoto and Rohr

Claims 1-3 and 5-11 were also rejected over a combination of Rohr in view of Tsujimoto. It was argued that Rohr discloses magnetic particles having binding members which include antibodies immobilized on the surface and their use in determining the presence of an analyte in the test fluid. Accordingly, it was argued that it would be obvious for one of ordinary skill in the art to use the antibodies of Tsujimoto et al. in the method of Rohr.

For the reasons indicated above Tsujimoto does not teach or render obvious the antibodies claimed within the presently pending claims. Tsujimoto et al. do not teach toward the use of partial peptides as immunogens to produce antibodies. Accordingly, even if Rohr and Tsujimoto are combined with each other there is no teaching of the claimed invention. Further, it is applicant's position that Rohr and Tsujimoto are not obviously combinable with each other and that they have been combined here by utilizing the hindsight provided by applicant's teachings.

Conclusion

Claims 2 and 4 are canceled and claims are amended in order to more particularly point out and distinctly claim the invention. The objection to the specification has been responded to with an

indication that applicant would be amenable to amending the specification should the objection be maintained. Each of the 35 U.S.C. §112, second paragraph rejections have been addressed by the presently amended claims which are believed to overcome the objections. Should the Examiner find that minor issues remain the Examiner is respectfully requested to contact the undersigned attorney to arrange for an interview to expedite the disposition of the application as applicant would be amenable to other amendments to place the specification or claims in condition for allowance. The combination of Gombinski and Tsujimoto et al. has been made by utilizing the hindsight provided by applicant's teachings. However, even the combination does not suggest that it is possible to evaluate renal function by first measuring megsin protein and then comparing the measured amount in the sample with the amount in the control specimen from a healthy individual in order to make a determination with respect to renal function. Further, Tsujimoto et al. do not teach producing antibodies using fragments of megsin protein and particularly with the fragments taught by applicant which fragments would be more effective in accurately measuring megsin protein due to their characteristics. Accordingly, even if Tsujimoto is combined with Rohr it does not teach applicant's invention. In view of such reconsideration and withdrawal of the rejections and allowance of the application is respectfully requested.

In the event that minor issues remain unresolved the Examiner is requested to contact the undersigned attorney at the indicated telephone number to arrange for an interview to expedite disposition of the application.

In the event other petitions are required or fees are necessary in connection with those petitions or other matters to maintain the pendency of the application, the Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number SHIM-012.

Respectfully submitted,
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